REMARKS

I. Amendment To The Title and Claims

The Title of the invention has been amended to describe the subject matter of the invention.

The specification has been amended to include specific dosage forms and dose ranges. Support for this amendment is found, for example, in U.S. Patent Application No. 10/392,195 (page 18, lines 2-27), which is incorporated by reference on page 25, lines 3-5 of the specification. Support for the dosage forms and dose ranges is also found in the specification on pages 32 and 43.

Claims 1, 2, 9, 23 and 27 have been amended and claims 6-8, 10-22 and 24-26 have been canceled without prejudice. Claims 28-31 have been added. Upon entry of the present amendments, claims 1-5, 9, 23 and 27-31 are pending in this application. No new matter has been introduced by the amendments, and their entry is respectfully requested.

Claims 1 and 23 have been amended to delete "preventing, modifying or managing" and to recite "complex regional pain syndrome" in place of "pain." Support for this amendment may be found, for example, in original claims 8 and 9 and on page 4, line 26 to page 6, line 28 of the specification.

Claim 1 and 23 have also been amended to replace "selective cytokine inhibitory drug" with "(+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}." Support for this amendment may be found, for example, in original claim 27.

Claim 2 has been amended to delete "or prophylactically."

Claims 9 and 27 have been amended to depend from claim 1.

Claim 27 has been amended to recite "compound" in place of "selective cytokine inhibitory drug."

New claims 28 and 29 are supported by, for example, original claim 1, and the specification at page 11, lines 7-9, page 32, lines 26-32 and page 48, lines 10-11.

New claim 30 is supported by, for example, original claim 1, and the specification at page 43, line 19 to page 45, line 30.

New claim 31 is supported by, for example, original claim 1, and the specification at page 43, lines 20-25 and page 44 lines 1-12.

New claims 32-34 are supported by, for example, the specification at page 32, lines 8-17, and the amendment to the specification at page 32, line 22.

By the amendments, Applicant does not acquiesce to the propriety of any of the Examiner's rejections and does not disclaim any subject matter to which Applicant is entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997). Further, Applicant reserves the right to prosecute the subject matter of any canceled or withdrawn claims in one or more continuation, continuation-in-part, or divisional applications.

II. Claims Objections under 37 C.F.R. § 1.75(c)

The Examiner objects to claim 27 as being an improper multiple dependent claim because it depends from a dependent claim. Claim 27 is deleted, and therefore, Applicant requests withdrawal of this objection.

III. Claims Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-6, 8-9, 23 and 27 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide an enabling disclosure. Specifically, the Examiner alleges that the specification does not enable "a method of preventing or modifying pain, or administering a prophylactically effective amount of a second agent." (Office Action, page 4). The Examiner, however, admitted that the specification is enabling for a method of treating neuropathic pain. (Id.).

Solely to promote the allowance of the case and without acquiescing to the Examiner's rejection, the claims have been amended to delete "preventing, modifying or managing pain," and "a prophylactically effective amount." Claims 6 and 8 have been canceled, therefore, the rejection of these claims is moot. As the Examiner himself admitted that the specification is enabling for a method of treating neuropathic pain, amended claims 1-5, 9, 23 and 27 are enabled.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *U.S. v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). The Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. Manual of Patent

Examining Procedure (hereafter "MPEP") § 2164.04, (citing *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993)). Furthermore, "[a] specification disclosure...must be taken as being in compliance with the enablement requirement...unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *Id.* (emphasis added).

The amended claims recite, *inter alia*, methods of treating complex regional pain syndrome by administering to a patient a specific compound, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. The specification clearly discloses that the recited disease can be treated with the recited compound. (*See, e.g.*, page 4, line 26 to page 6, line 28; page 18, last paragraph to page 19, first paragraph; and page 25, lines 9-11). It is also disclosed that the recited compound can be prepared by synthetic procedures, as described in the specification. (*See, e.g.*, page 25 line 19 to page 26, line 2). Dosages and routes of administration of the compound are disclosed, for example, on page 32, lines 8-22 of the specification.

Therefore, all that is required for those of ordinary skill in the art to practice the claimed invention is to administer the specified amount of the recited compound using the specified routes of administration. In view of the foregoing, the specification provides a sufficient guidance as to treating complex regional pain syndrome. Thus, one skilled in the art would have been able to make or use the claimed invention without undue experimentation.

Next, claims 2-5 recite methods of treating complex regional pain syndrome by administration of a specific compound, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}, with a second active agent. The claims are fully supported by the specification. The specification discloses examples of conventional therapeutics that can be used as second active agents to treat pain. (*See, e.g.*, page 28, line 26 to page 29, line 30; page 30, lines 3-14). The specification further discloses methods of combination therapy in which a second active agent may be used with (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. (*See, e.g.*, page 28, line 13 to page 30, line 14).

Applicant respectfully submits that the use of a second active agent for use with the compounds recited in the instant claims would require only routine experimentation. Merely routine experimentation is not undue. *See In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir 1988). The determination by a physician as to whether any agent is effective in

treating a disease in a given patient is a routine practice and is always performed for every pharmaceutical. The specification provides a detailed description of using the second active agent in the combination therapy. (*See, e.g.*, page 34, line 15 to page 39, line 2). The specification teaches which agents to use, and how much of the agents are used. (*See, e.g.*, page 34, lines 30 to 36; page 35, lines 1-18). One of ordinary skill in the art, armed with the information presented in the specification, has adequate guidance to practice the claimed invention. Applicant respectfully submits that one reasonably skilled in the art could make or use the invention as claimed without undue experimentation.

In sum, Applicant respectfully submits that: (1) the specification provides sufficient information and guidance to those of ordinary skill in the art to make and use the claimed invention; (2) the Examiner did not provide any factual or legal basis to doubt that the claims are enabled; and (3) to the extent any experimentation is necessary, such experimentation is not undue. Therefore, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

IV. Claims Rejections under 35 U.S.C. § 102

A. Claims 1, 6, 8 and 9 are not anticipated by Rajkumar, *et al.*

Claims 1, 6, 8 and 9 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Rajkumar, *et al.*. The Examiner alleges that claims 1, 6, 8 and 9 are anticipated because Rajkumar teaches the use of thalidomide to treat complex regional pain syndrome. (Office Action, page 14). Applicant respectfully disagrees.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131 (*citing Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).

Rajkumar purportedly reports the use of thalidomide to treat reflex sympathetic dystrophy, also known as complex regional pain syndrome, in a single patient. Instant claim 1 recites the use of a specific compound, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}, to treat complex regional pain syndrome. Thus, Rajkumar is missing the essential element of the claimed invention- the use of a specific compound, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}.

Therefore, the alleged teachings of Rajkumar cannot anticipate claim 1 because it fails to teach the claimed method for treating a specific disorder using a specific compound in a specific amount. Claims 6 and 8 are canceled, thus the rejection is moot as to these claims. Because claim 9 depends from claim 1, it is not anticipated by Rajkumar. Applicant respectfully requests that the rejection by Rajkumar be withdrawn.

B. Claims 1 and 6 are not anticipated by Olmarker, *et al.*

Claims 1 and 6 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Olmarker, *et al.* (U.S. Patent No. 6,635,250). The Examiner alleges that the claims are anticipated because Olmarker discloses a method of using a TNF-α inhibitor to treat neuropathic pain. (Office Action, page 15). Applicant respectfully disagrees.

Instant claim 1, as currently amended, recites a method of treating complex regional pain syndrome using (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. Olmarker allegedly teaches use of a TNF-α inhibitor in treating nerve root injuries, without mentioning the specific compound of claim 1, or complex regional pain syndrome. Because Olmarker does not disclose methods of treating complex regional pain syndrome using the specific compound of claim 1, claim 1 is not anticipated by Olmarker.

Claim 6 has been canceled. Therefore, the rejection by Olmarker should be withdrawn.

V. Claims Rejections under 35 U.S.C. § 103

A. Claims 2-5 and 23 are Patentable over Rajkumar, *et al.* in view of Merck.

Claims 2-5 and 23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Rajkumar, *et al.*, in view of the Merck Manual. (Office Action, pages 15-16).

Under the current law, prior art references cannot render a claim obvious unless the PTO provides evidence that the references meet a three-part test for *prima facie* obvious. To begin with, the prior art reference or references must provide "motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant." *See In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000); *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 2005). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See In re Kotzab*, 217 F.3d at 1370, 55 U.S.P.Q.2d at 1316-17. Where

an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355, 51 U.S.P.Q.2d 1385, 1397 (Fed. Cir. 1999); *Princeton Biochemicals, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d at 1054; *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002).

Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988); *Boehringer Ingelheim Vetmedica, Inc.*, 320 F.3d 1339, 1354, 65 U.S.P.Q.2d 1961, 1971 (Fed. Cir. 2003); *Noelle v. Lederman*, 355 F.3d 1343, 1352, 69 U.S.P.Q.2d 1508, 1516 (Fed. Cir. 2004). Further, "[b]oth the suggestion and the reasonable expectation of success 'must be founded in the prior art, not in the applicant's disclosure.'" *Noelle*, 355 F.3d at 1352, 69 U.S.P.Q.2d at 1515-16 (quoting *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991)). Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1569, 39 U.S.P.Q.2d 1321, 1327 (Fed. Cir. 1996).

The Examiner alleges that claims 2-5 and 23 are obvious because Rajkumar teaches the use of thalidomide to treat complex regional pain syndrome, and Merck discloses that certain drugs, physical therapy and/or surgery can be used to treat complex regional pain syndrome. (Office Action, page 15). Applicant respectfully disagrees.

The claimed invention is directed to methods of treating complex regional pain syndrome using a specific compound, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. Rajkumar is silent as to (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. Rajkumar does not provide to one skilled in the art any suggestion or motivation to select any compound other than thalidomide, not to mention the isomer of a specific racemic compound disclosed in instant claim 1, to treat complex regional pain syndrome.

Furthermore, Rajkumar does not disclose or suggest using any selective cytokine inhibitory drug. As the present invention discloses, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione} is a

selective cytokine inhibitory drug. Therefore, one skilled in the art would not be motivated to select the specific selective cytokine inhibitory drugs as recited in the instant claims, based on the purported teaching of Rajkumar. Moreover, as the Examiner mentions, Rajkumar discloses nothing about the use of a second therapeutic agent. (Office Action, page 15).

Second, regarding the teachings of Merck in view of Rajkumar, Merck adds nothing to the disclosure of Rajkumar, because neither Rajkumar nor Merck would provide a suggestion or motivation to one skilled in the art to treat complex regional pain syndrome with the specific compound disclosed in claim 1, in combination with a second therapeutic agent, treatment or surgery.

Because the Examiner has provided no evidence of a teaching, suggestion or motivation for one skilled in the art to select the compound of claim 1 for the treatment of complex regional pain syndrome, the instant claims cannot, and are not, rendered obvious by Rajkumar in view of Merck.

Next, the references cited by the Examiner do not suggest to one of ordinary skill in the art that the present invention would have a reasonable expectation of success. *See In re Dow Chemical*, 837 F.2d at 473. Neither Rajkumar no Merck disclose the specific compound of the instant claims, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. Rajkumar merely discloses thalidomide. As is known to one skilled in the art, even slight modifications in structure can have substantial effects on the properties of a compound. Further, alleged obvious differences in specific chemical structures must be adequately supported in the prior art. *See* MPEP § 2144.09, citing *In re Grabiak*, 769 F.2d 729, 731-32, 226 U.S.P.Q. 871 (Fed. Cir. 1985). The structural differences between thalidomide and the compound of the instant claims are significant, and one skilled in the art would not be able to predict whether (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione} would be useful to treat complex regional pain syndrome in view of the teachings of Rajkumar. For these reasons, in view of Rajkumar and Merck, one skilled in the art would have no reasonable expectation that the specific compound of claim 1 would be successful in the treatment of complex regional pain syndrome.

Finally, the Examiner has not met his burden of establishing that the prior art references, either alone or in combination, teach or suggest each and every limitation of

the instant claims. *See Motorola, Inc.*, 121 F.3d at 1473. Again, Rajkumar and Merck do not disclose the specific compound of the instant claims, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. The use of thalidomide as purportedly related in Rajkumar together with the combination therapies allegedly outlined by Merck is not enough to suggest the use of the specific compound of claim 1, in combination with another therapeutic agent, to treat complex regional pain syndrome.

The Examiner, relying merely on conclusory remarks, has not provided factual, objective evidence to support his assertion that claims 2-5 and 23 are obvious in light of Rajkumar and Merck. *See In re Sang-Su Lee*, 277 F.3d 1338, 1343-44 (Fed. Cir. 2002). Therefore, the rejection of claims 2-5 and 23 should be withdrawn.

B. Claim 27 is Patentable over Olmarker, *et al.* in view of Muller, *et al.*

Claim 27 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Olmarker in view of Muller, *et al.* (U.S. Patent No. 6,020,358, "Muller"). (Office Action, page 17). Applicant respectfully disagrees.

Claim 27 recites, *inter alia*, a method of treating complex regional pain syndrome by the administration of (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. Olmarker discloses "thalidomide derivatives, e.g., SelCID, i.e. Selective Cytokine inhibitors," without teaching or suggesting a specific compound or its use as recited in the present claims. (Page 7, line 24). The mere fact that a claimed species is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *See* MPEP § 2144.08; *In re Baird*, 16 F.3d 380, 382, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994).

Muller discloses, at a minimum, certain methods of reducing undesirable levels of TNF-α. However, Muller fails to teach or suggest the claimed methods of treating a specific disease of complex regional pain syndrome.

Neither Olmarker nor Muller, alone or in combination, suggest methods of treating complex regional pain syndrome, not to mention the claimed methods using the specific compound of claim 27. Nothing in Olmarker suggests that the methods disclosed therein should be adapted to treat any other disease or disorder beyond the treatment of nerve root injuries, not to mention the specific disorder of claim 27, complex regional pain syndrome, much less using the recited compound. Muller fails to disclose or suggest

methods of treating complex regional pain syndrome, not to mention the method of treating complex regional pain syndrome with the specific compound of claim 27.

The Examiner has not shown how one skilled in the art, reading Muller in view of Olmarker, would arrive at the particular method of claim 27. Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc.*, 184 F.3d at 1355. No suggestion or motivation exists to combine Muller with the methods of Olmarker to arrive at the specific method of instant claim 27, treatment of complex regional pain syndrome.

Furthermore, the references cited by the Examiner do not suggest to one of ordinary skill in the art that the method of the present invention for treating complex regional pain syndrome would have a reasonable expectation of success. *See In re Dow Chemical*, 837 F.2d at 473. Because neither Muller nor Olmarker teach or suggest methods of treating complex regional pain syndrome, one skilled in the art would have no reason to expect that (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione} would be useful in treating complex regional pain syndrome.

Finally, the Examiner has not met his burden of showing that Muller and Olmarker teach or suggest each and every element of the instant claims. *See Motorola*, 121 F.3d at 1473. An essential element of claim 27, treating complex regional pain syndrome, is not taught by Muller or Olmarker.

In sum, the Examiner has not presented any evidence to show that one skilled in the art, reading Olmarker in view of Muller, would be motivated to select (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione} from Muller and use that compound to treat complex regional pain syndrome. *See Baird,* 16 F.3d at 382. Therefore, the rejection of claim 27 under 35 U.S.C. § 103(a) should be withdrawn.

C. Claims 2-5 and 23 are Patentable over Olmarker, *et al.* in view of Merck.

Claims 2-5 and 23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Olmarker in view of Merck. The Examiner alleges that instant claims are obvious because Olmarker discloses a method of using a TNF-α inhibitor to treat nerve root injuries, and Merck discloses that certain drugs, physical therapy and/or surgery can be used to treat complex regional pain syndrome. (Office Action, page 18).

Olmarker does not suggest using the specific compound of claim 1 with an additional agent or therapy. Moreover, Olmarker does not suggest any methods of treating complex regional pain syndrome, much less the specifically claimed combination therapy. In sum, it has not been established that Olmarker suggests the essential elements of the claimed invention herein, *e.g.*, the claimed methods using a specific compound with other agent for treating complex regional pain syndrome. That is, Olmarker is missing any teaching or suggestion of essential elements of the claimed invention.

Merck does not cure the deficiency of Olmarker. Merck allegedly discloses that certain drugs, physical therapy and/or surgery may be used to treat complex regional pain syndrome. However, Merck does not suggest the use of the specific compound for treating complex regional pain syndrome, much less a combination with another drug or therapy as claimed.

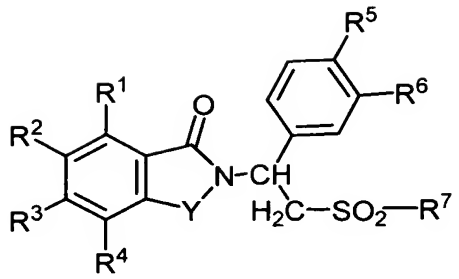
The Examiner has identified no teaching or suggestion that the recited compound may be used in treating pain, much less complex regional pain syndrome, much less the combination therapy. Nowhere does Olmarker or Merck suggest or motivate the use of the recited compound with additional agent or therapy for treating pain, let alone complex regional pain syndrome. Thus, one of ordinary skill in the art would not have had a reasonable expectation of success from Olmarker and Merck. A *prima facie* case of obviousness has not been established and the rejection must be withdrawn.

IV. Obviousness-Type Double Patenting Rejections

Claims 1, 6 and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claim 17 of U.S. Patent No. 6,020,358 ("the '358 patent"), or claim 15 of U.S. Patent No. 6,011,050 ("the '050 patent") in view of claims 1, 21 and 27 of U.S. Patent No. 6,635,250 ("the '250 patent"). Applicant respectfully disagrees.

An obviousness-type double patenting rejection is appropriate only when the claims at issue are not "patentably distinct" from the claims of a commonly owned earlier patent. *See Eli Lilly & Co. v. Barr Laboratories, Inc.*, 251 F.3d 955, 967 (Fed. Cir. 2001).

The claims of the '358 patent and the '050 patent are drawn to methods of reducing undesirable levels of TNF-α in a mammal by administering a species and genus compound of the formula:



wherein Y is C=O, CH_2, SO_2, or $CH_2C=O$; R^1, R^2, R^3, R^4, R^5, R^6 and R^7 encompass a diverse variety of substituents. Claims 1, 21 and 27 of the '250 patent relate to methods of treating a nerve disorder caused by a herniated disc with a TNF-α inhibitor, metalloproteinase inhibitor.

The recited patents do not disclose or suggest the specific disease of the instant claims, complex regional pain syndrome, as admitted by the Examiner himself. (Office Action, page 19).

The pending claims, as amended, recite the use of a specific compound, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}, for treating complex regional pain syndrome. Therefore, the subject matter of the claims of the patents and the instant application are not encompassed by each other and are patentably distinct. The rejection over the cited patents must be withdrawn.

The Examiner also rejected claims 1 and 6 as unpatentable over the claims of any of 12 issued U.S. patents (US Patent Nos. 5,635,517; 5,955,476; 5,798,368; 5,698,579; 5,736,570; 5,703,098; 6,395,754; 6,180,644; 6,130,226; 6,075,041; 6,214,857; 5,968,945) in view of the '250 patent (Office Action, pages 20-21). Applicant respectfully disagrees.

The 12 patents cited by the Examiner are drawn to methods of reducing undesirable levels of TNF-α in a mammal using TNF-α inhibitors. Claims 1, 21 and 27 of the '250 patent relate to methods of treating a nerve disorder caused by a herniated disc with a TNF-α inhibitor, metalloproteinase inhibitor.

The instant claims, as amended, are directed to methods of treating complex regional pain syndrome, using a specific compound, (+)-{2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione}. The Examiner himself stated that none of the 12 patents cited in combination with the '250 patent disclose or claim a method of treating neuropathic pain, not to mention the specific disorder of complex regional pain syndrome. (Office Action, page 21). The cited patents do not disclose or suggest methods of treating complex regional pain syndrome using a

specific compound as claimed in the present application. Therefore, the pending claims in the present application are patentably distinct from the claims of the cited patents.

In sum, Applicant respectfully submits that the rejection of the pending claims under obviousness-type double patenting should be withdrawn because no *prima facie* case of obviousness has been established for the pending claims over any of the cited patents. Applicant further submits that no terminal disclaimer over the cited patents is necessary.

Conclusion

In view of the foregoing, all the rejections of the claims should be withdrawn. Reconsideration, entry of the above amendment and remarks, and allowance of the pending claims are respectfully requested. Should the Examiner not agree that all claims are allowable, a personal or telephonic interview is respectfully requested to discuss any remaining issues and to accelerate the allowance of the above-identified application.

Please apply fees for the Extension of time and any other charges, or any credits, to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Date: March 12, 2007

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